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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,957	01/11/2001	Robert N. Hanson	ZAA-011.01	9648

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FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 06/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/758,957

Applicant(s)

HANSON ET AL

Examiner

Jon D. Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15,55,56 and 58-62 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☒ Claim(s) 61 and 62 is/are allowed.
6) ☒ Claim(s) 15,55,56 and 58-60 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Status of the Application

1. The Response filed March 7, 2005 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 15 and 55-62 were pending. Applicants canceled claim 57 and amended claims 15, 58, 59, 60, 61 and 62. Therefore, claims 15, 55, 56 and 58-62 are currently pending and examined on the merits.

Withdrawn Objections/Rejections

4. The Dutta et al. rejection under 35 U.S.C. § 102 is withdrawn in view of Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112

5. Claims 15, 55, 56 and 58-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not provide support for the invention as now claimed. The specification as originally filed includes only two specific structures that would read on the presently claimed generic (i.e. Figure 9, bottom two compounds). This is deemed to be insufficient support for the newly recited generic that encompasses a wide variety of compounds outside of those compounds presented in Figure 9 (please note that generic formula II does not appear anywhere in the specification and/or the original set of claims). For example, consider just the members of the proposed Markush group for R_1 . The two compounds of Figure 9 contain a $-\text{CO}_2\text{H}$ group at this position only. So, there is only support for the proposed $R_1 = -\text{CO}_2\text{R}_4$ where $\text{R}_4 = \text{H}$ i.e., Applicants only provide support for $R_1 = -\text{CO}_2\text{H}$. However, R_4 also recites alkyl. The $-\text{CO}_2(\text{H})$ is not sufficient support for $-\text{CO}_2(\text{alkyl})$. For example, hydrogen and alkyl groups are NOT bioisosteres (i.e., interchangeable) because they have different size, shape, electronic distribution, lipid solubility, water solubility, pK_a , chemical reactivity, and hydrogen bonding (e.g., see Silverman et al., pages 19-23). For example, an alkyl group attached to a carboxylic acid (i.e., the "R" portion of the $-\text{CO}_2\text{R}$ ester group) cannot undergo hydrogen bonding like the hydrogen atom that is attached to a carboxylic acid can (i.e., the "H" portion of the $-\text{CO}_2\text{H}$ acid group). In addition, the alkyl groups are larger than the hydrogen and more lipophilic and have much higher pK_a values. Thus, Applicants' example of a hydrogen atom at the R_4 position does not provide support for an alkyl group at this same position because these groups would have significantly different physiochemical properties (as mentioned above) and thus do not have similar structural features and/or reactivity. Moreover, the H/F atoms in the

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para positions of the ZHN-94/ZHN-94 phenyl rings (e.g., see figure 9) do not supply support for Cl, Br or I in those positions. For example, Silverman shows that only H and F are bioisosteres (i.e., interchangeable), not H, F, Cl, Br and I (e.g., see Silverman, Table 2.3, entry 11 showing the interchangeability of H and F). In addition, the H in the ortho and meta positions of the GBR 12935 phenyl rings do not supply support for H, F, Cl, Br or I in those positions (e.g., see Silverman, Table 2.3, entry 11 showing interchangeability of H and F).

For example, with respect to the “-F” substituents at the *ortho*, *meta* and *para* position of the phenyl rings (e.g., see newly amended claim 15) the Examiner contends that Applicants have not provided any “identifying” language that would encompass the claimed genus (e.g., Applicants do not state in the specification that a “halogen” can be substituted at the *ortho*, *meta* and *para* positions). For example, in *In re Grimme, Keil, and Schmitz* 124 USPQ 499 (CCPA 1960) the Court held that naming one member of a chemical genus (i.e., a single species) is not, in itself, proper basis for a claim to an entire chemical genus unless the genus is sufficiently identified in the application by other appropriate language (e.g., see *In re Grimme, Keil and Schmitz* 124 USPQ 499, 501) (“On the other hand, in the case of a small and closely related group such as the halogens, the naming of the group should ordinarily be sufficient since nothing of consequence would be added by also naming each of the well known members of the group”). Here, Applicants failed to “name the group” and thus do not provide any “identifying” language (e.g., halogen) that would support the claimed genus. Therefore, the disclosure of a single species (i.e., the “F” atom) in the *ortho*, *meta* and *para* positions of the phenyl rings fails to satisfy the test set forth in *In re Grimme, Keil and Schmitz*. Likewise, there is no “identifying” language that would allow a person to extend the disclosure of the -CO₂H at the R₁ position to

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the currently claimed $\text{-CO}_2(\text{alkyl})$ (e.g., see *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000) wherein the CAFC stated, “Ruschig [referring to *In re Ruschig* 379 F.2d 990, 154 USPQ 118 (CCPA 1967)] makes clear that one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say “here is my invention.” In order to satisfy the written description requirement, the blazemarks directing the skilled artisan to that tree must be in the originally filed disclosure.”). Here, the Examiner cannot find any such “blazemarks” for Applicants’ currently claimed $\text{R}_1 = \text{-CO}_2(\text{alkyl})$ or $\text{R}_2/\text{R}_3 = \text{halogen}$ in the original disclosure as exemplified above.

Response

6. Applicant’s arguments directed to the above New Matter rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants’ newly amended and/or added claims and/or arguments.

[1] Applicants argue, “the Examiner may not rely on *In re Grimme*, *Keil*, and *Schmitz* 124 USPQ 499 (1960) in support of the contention that the description of a single compound is never sufficient to support a claim to a genus, regardless of the size of the genus.” Applicants further state that such a reading of *Grimme* conflicts with cases like *Enzo* because *Enzo* permits the use of “only one species” in certain situations to describe a genus (e.g., see 3/7/05 Response, page 8).

[2] Applicants argue that questions of possession must be determined on a “case-by-case” basis, which presumably lessens the weight of decisions like *In re Lukach* and *In re Smith* (e.g., see 3/7/05 response, page 9, middle paragraph).

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[3] Applicants argue, “synthesizing and describing the fluorophenyl compound is sufficient to establish that Applicants were in possession of halophenyl because a fluoro substituent is recognized as a halogen, which group also includes Cl, Br, and I ... in addition, there is no evidence that the compounds of the invention would be operable only with fluorophenyl” (e.g., see 3/7/05 Response, paragraph bridging page 9-10).

[4] Applicants argue, “that carboxylic acid is adequate to ‘reflect the [structural] variation within the genus] encompassing only carboxylic acid and its alkyl esters given the structural similarity of the two functional groups” and cite MPEP § 2163.05 in support of this position (e.g., see 3/7/05 Response, page 10, paragraph 2).

[5] Applicants argue, “a carboxylic acid can be converted to an ester. Thus, the Applicants contend that synthesizing and describing the carboxylic acid in combination with stating that the carboxylic acid may be converted to an ester conveys with reasonably clarity that the Applicants were also in possession of alkyl ester” (e.g., 3/7/05 Response, page 10, paragraph 2).

This is not found persuasive for the following reasons:

[1] The Examiner has never relied on *In re Grimme*, *Keil* and *Smitz* for the proposition that disclosure of a single compound is “never sufficient” to support a claim to a genus as purported by Applicants. The question of whether a single species can support a genus is simply not at issue in this case. The issue is whether Applicants’ original disclosure provides support for what is now claimed. Here, Applicants have not pointed to anything in the specification that provides support for $R_1 = -CO_2(\text{alkyl})$ and $R_2/R_3 = \text{halogen}$. Thus, Applicants’ arguments with

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regard to *Enzo*; *In re Grimme, Keil, and Schmitz*; *In re Rasmussen* and MPEP § 2163.05 are moot.

[2] The Examiner agrees that compliance with the written description requirement must be determined on a case-by-case basis, but notes that the great weight of the case law favors the Examiner's position (e.g., see *In re Lukach*; *In re Smith*; *In re Grimme, Keil and Schmitz*; *Purdue Pharma L.P. v. Faulding Inc.*; *In re Ruschig*) and further contends that the facts "in this case" also favor the Examiner's position as set forth in the newly amended rejection above.

[3] The Examiner respectfully disagrees. The prior art recognizes that the physiochemical properties of fluorine are more similar to hydrogen than to chlorine, bromine and iodine (e.g., see Silverman, Table 2.3, entry 11). Thus, a person of skill in the art would group fluorine with hydrogen, not with chlorine bromine and iodine. It should also be noted that Applicants have not even made an argument for the R₃ position, which is not substituted with fluorine (i.e., Applicants would have to argue that hydrogen falls with the art recognized class of halogen as well, which is clearly not the case).

[4] The Examiner respectfully disagrees. Applicant's arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Here, Applicants provide no evidence to support the contention that a carboxylic acid and an ester would be "structurally related." Furthermore, Applicants have not refuted (with any factual evidence) the Silverman reference, which clearly shows that a carboxylic acid is not structurally related enough an ester such that they would be considered interchangeable (i.e., they are not bioisosteres). Consequently, the Evidence simply does not support Applicants' position.

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[5] The Examiner contends that “obviousness” is not the standard (e.g., *Lockwood v. American Airlines, Inc.* 41 USPQ 2d 1961 at 1966 (CAFC 3/4/97) wherein the Court held that disclosure in an application that merely renders the later-claimed (by amendment) invention obvious is not sufficient to meet the written description requirement of 35 USC 112, first paragraph). Thus, the mere fact that a person of skill in the art might know how to convert an acid into an ester (i.e., it is an “obvious” procedure) is not relevant to the issue of possession.

In addition, to the extent that applicants are somehow arguing that the statements on the last paragraph of page 12 of the specification lend support for the currently claimed ester compounds, the Examiner notes that Applicants only refer to the use of an ester in the context of a “laundry list” of potential protecting groups, which the Court has rejected time and time again as providing support for a more narrowly drawn genus or subgenus (e.g., see, *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a “laundry list” disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not “reasonably lead” those skilled in the art to any particular species); see also *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) (“If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.”) (emphasis in original); see also *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) (“the specification does not clearly disclose

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to the skilled artisan that the inventors ... considered the ratio... to be part of their invention

There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion"). Here, Applicants' broad disclosure of the use of an ester as "protecting group" for presumably any compound would not reasonably convey to a person skilled in the art to make the claimed ZHN-94 and GBR 12935 acid/ester substitutions leading to the currently claimed subgenus.

Accordingly, the New Matter rejection cited above is hereby maintained

Allowable Subject Matter

7. Claims 61-62 are allowable.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

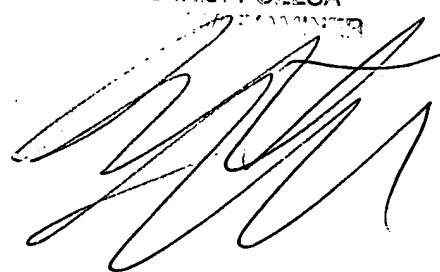
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
May 23, 2005

BENNETT CELSA
EXAMINER

A handwritten signature in black ink, appearing to read 'Bennett Celsa', is written over the printed name and title. The signature is stylized with large, sweeping loops.